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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/991,209	11/16/2001	Nigel Dunn-Coleman	GC648-2	6062

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GENENCOR INTERNATIONAL, INC.
ATTENTION: LEGAL DEPARTMENT
925 PAGE MILL ROAD
PALO ALTO, CA 94304

EXAMINER	
KALLIS, RUSSELL	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 11/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/991,209	DUNN-COLEMAN ET AL.	
	Examiner	Art Unit	
	Russell Kallis	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,18,19,23,25,27-33 and 74* is/are pending in the application.

4a) Of the above claim(s) *57* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15,18,19,23,25,27-33 and 74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *02/23/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 16-17, 20-22, 24, 26, 34-56 and 58-73 are cancelled. Claims 1-15, 18-19, 23, 25, 27-33 and 74 are pending and examined. Claim 57 is withdrawn.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Rejection of Claims 1-2, 8 and 13-15 under 35 U.S.C. 103(a) is withdrawn in view of Applicant's amendments and arguments.

Rejection of Claims 3-7, 15, 18-19, 27-28 under 35 U.S.C. 112, 2nd paragraph is withdrawn in view of Applicant's amendments and arguments.

Election/Restrictions

This application contains Claim 57 drawn to an invention nonelected with traverse in Paper No. 11/03/03. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01. Claims 18-19 and 57 of invention B were included in the election, but Claim 57 is drawn to the non-elected invention of Group II and is withdrawn from examination, while Claims 18-19 are drawn to the elected invention of Group I and are examined.

Claim Rejections - 35 USC § 112

Claims 1-15, 18-19, 23, 25, 27-33 and 74 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is maintained for the reasons of record set

forth in the Official action mailed 2/17/04. Applicant's arguments filed 8/16/04 have been fully considered but they are not persuasive.

Applicant asserts that they are not required to describe each and every embodiment of the presently claimed invention to describe a representative number of a species (response page 7, under 35 U.S.C. 112 1st paragraph lines 10-11). Although each and every embodiment need not be described, from Applicant's lack of written description of the claimed genus it remains unclear what features identify a ferulic acid esterase encoding polynucleotide.

Applicant further asserts, "For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus" (response page 7, under 35 U.S.C. 112 1st paragraph, lines). However, Applicant has only described a single cDNA encoding a ferulic acid cDNA from *Aspergillus* of SEQ ID NO: 1, and thus fails to describe structural features common to members of the claimed genus of polynucleotides essential for a ferulic acid esterase activity. Since the genus of ferulic acid esterase encoding polynucleotides has not been described by specific structural features, the specification fails to provide an adequate written description to support the breath of the claims.

Claims 1-15, 18-19, 23, 25, 27-33 and 74 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for transgenic Festuca and Lolium comprising a polynucleotide encoding an FAE1 enzyme from *Aspergillus* wherein expression of the *Aspergillus* FAE1 is targeted to the vacuole, ER, or apoplast, does not reasonably provide enablement for any plant comprising any FAE1 encoding polynucleotide from any organism. The specification does not enable any person skilled in the art to which it pertains, or with which

it is most nearly connected, to make the invention commensurate in scope with these claims. This rejection is maintained for the reasons of record set forth in the Official action mailed 2/17/04. Applicant's arguments filed 8/16/04 have been fully considered but they are not persuasive.

Applicant asserts since a ferulic acid esterase may be isolated using the methods of U.S. Patent 6,368,833 and given the teachings of the specification each and every embodiment of the specification could be isolated (response page 8 lines 1-10). The claims are drawn to transformed plants expressing a ferulic acid esterase and although ferulic acid esterase can be isolated it would be undue experimentation to test for activity in a multitude of non-exemplified transformed plant species.

Applicant asserts that the invention is pioneering and that given the disclosure of the specification one of skill in the art could isolate other naturally occurring FAE encoding polynucleotides and easily avoid claims drawn narrowly to specific sequences (response page 8 lines 12-23). Applicant has not taught how to use the claimed transformed plants. Applicant has broadly claimed a plant comprising a ferulic acid esterase encoding polynucleotide linked to a vacuolar targeting sequence, further comprising a xylanase encoding polynucleotide, but only teaches transformation of Festuca and Lolium (i.e. grasses) with a polynucleotide encoding an FAE1 enzyme from *Aspergillus*, wherein expression of the *Aspergillus* FAE1 is targeted to the vacuole, ER, or apoplast (Examples 3-5, pages 38-40) and does not teach any other plants comprising any other ferulic acid esterase encoding polynucleotides other than Festuca and Lolium comprising the *Aspergillus* FAE1 encoding polynucleotide. Applicant has not responded to the enablement rejection about the unpredictability of identifying a ferulic acid esterase

encoding polynucleotide that would have activity in the plant, which is illustrated in experiments where a polynucleotide believed to encode a ferulic acid esterase showed no activity towards an esterified ferulic acid (Kroon P. *et al.* Biochemical Society Transactions, 1998; Vol. 26; page S167, column 2, second paragraph). Although the ferulic acid esterase encoding polynucleotide isolated from *Aspergillus niger* showed activity for ferulic acid esterified to C5 of arabinofuranose found in cereals and grasses but showed no activity towards ferulic acid esterified to the C2 and C6 residues of arabinofuranse and galactopyranose residues respectively, typical of esterified ferulic acid found in sugar beet.

Applicant asserts that they have incorporated through reference to WO 98/14594 enzymes useful in the present invention (response page 8, lines 28-29). Application WO 98/14594 is a priority document of U.S. Patent 6,368,833 dos not describe or teach how to use multiple ferulic acid enzymes it teaches isolation of one polynucleotide encoding one ferulic acid esterase enzyme isolated from *Aspergillus* (See Abstract).

Given the unpredictability in the art as to which ferulic acid esterase encoding polynucleotides would have activity upon a conjugated ferulic acid substrate associated with a particular plant species; the breadth of the claims encompassing any ferulic acid esterase encoding polynucleotide; the lack of guidance in the examples of the specification or in the prior art; undue trial and error experimentation would be needed by one skilled in the art to make and clone a multitude of non-exemplified ferulic acid esterase encoding polynucleotides and would require one of skill in the art to test in a myriad of non-exemplified plants for an altered phenotype in a multitude of non-exemplified transformed plant species. Therefore, the invention is not enabled for the scope set forth in the claims.

Claims 2, 8, 14, 25, 27-29 and 74 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In Claim 2, "derived" is indefinite. It is unclear what has been changed and what has been preserved in the derivation.

Applicant asserts that the specification defines "derived" on pages 9-10, and thus the use of derived is not indefinite. The use of the term derived in the claims suggests that the polynucleotide sequence is isolated from the organism from which the claims states it is derived i.e. derived from *Aspergillus*. This does not match the stated definition in the specification which states that the term derived means homologous to another sequence, either in the natural (i.e. across species or different isoforms) or man made sense (i.e. introduced mutations), which is to say there is some sequence variation. Claim 2 simply states that the polynucleotide is derived from an organism, not another sequence.

In Claim 8, "the introduction of the ferulic acid esterase polynucleotide", lacks proper antecedent basis.

In Claim 14, "the N-terminus" typically refers to the amino end of a polypeptide. The claim is drawn to a polynucleotide. The ends of polynucleotides are referred to as the 5' and 3' ends. The Examiner suggests that following 5' with a noun such as "end" would obviate this rejection.

In Claim 25 "the C-terminus" is typically used to refer to polypeptides; i.e. the carboxy terminus. The claim is drawn to a polynucleotide. The ends of polynucleotides are referred to as

the 5' and 3' ends. The Examiner suggests that following 3' with a noun such as end would obviate this rejection.

In Claims 27 and 28, "the polynucleotide sequence" refers back to "the polynucleotide sequence" of Claim 25 that refers back to "the polynucleotide sequence" of Claim 13 which is a target sequence. It is unclear how "the polynucleotide sequence" could be both a target sequence and the claimed stop codon or extension/linker sequences of Claims 27 or 28 respectively. Applicant asserts that the signal sequence can be placed at the 3' end of the coding sequence as well. The Examiner suggests that the word "is" in line 1 of both Claims 27 and 28 be changed to "further comprises" to show that the polynucleotide encoding the signal sequence and the stop codon of Claim 27 are both included in the claim and similarly for the linker sequence of Claim 28.

In Claim 29, "further comprising introduction into a plant", is rejected for reciting the positive method step. The Examiner suggests that deleting "introduction into the plant" would obviate this objection.

In Claim 74, line 2, there is no antecedent basis for "the plant". Amending the claims to recite --a plant-- would obviate this rejection.

Claim Rejections - 35 USC § 102

Claims 1-2, 8, 13-14 and 23 remain rejected under 35 U.S.C. 102(a) as being anticipated by Michelson B. *et al.* U.S. Patent 6,143,543 issued November 7, 2000. This rejection is maintained for the reasons of record set forth in the Official action mailed 2/17/04. Applicant's arguments filed 8/16/04 have been fully considered but they are not persuasive.

Applicants asserts that the teachings of Michelson are not enabling for production of an enzyme in a plant because of the need to remove the intron from the *Aspergillus* sequence, the need to modify the FAE sequence to match the codon usage of plants, and the need to target the FAE expression to a particular cell compartment (response page 11). There is no evidence to suggest that the FAE and the techniques taught in the specification of Michelson would not result in the stable expression of FAE in a transformed plant. Further, since, splicing machinery is conserved among eukaryotes and codon usage would not prevent expression of a fungal sequence in a plant, both the presence of an intron and non-plant optimized codons would not prevent expression of the fungal FAE in a plant. Furthermore, the *Aspergillus* sequence of the '543 Patent, known in the art, inherently teaches a signal sequence; see the first non-patent publication listed in references cited, de Vries et al., on page 4640 column 2.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2, 8-14, 23, 25, 27-29, 31 and 74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Michelson *et al.* U.S. Patent 6,143,543 issued November 7, 2000 in view of Bartolome B. *et al.*, Applied and Environmental Microbiology; January 1997, pages 208-212.

Applicant broadly claims a plant comprising both ferulic acid esterase encoding and xylanase encoding polynucleotides linked to an ER retention signal (KDEL) and either an inducible, senescence, heat shock, or constituitive promoter.

Michelson teaches a polynucleotide encoding a ferulic acid esterase (FAE III) from *Aspergillus niger* (columns 8-9), methods of plant transformation (columns 16-17 and 21-22), a plant comprising an expression cassette comprising a ferulic acid esterase encoding polynucleotide in plants derived from *Aspergillus niger*, operably linked to a promoter, taught as an embodiment of the invention (see Column 6, lines 20-21, column 8 lines 30-31 and column 10 lines 24-29); and the expression of the ferulic acid esterase and xylanase together demonstrated by the release of ferulic acid and diferulate dimers from cell walls of wheat (column 27, lines 3-11 and column 28, lines 21-28; and page 16 of the specification).

Michelson does not teach a polynucleotide encoding a xylanase.

Bartolome teaches recombinant expression cassettes comprising XylD and XylA (page 208, column 2 in Materials and Methods) and that a xylanase in combination with a ferulic acid esterase from *Aspergillus niger*, together more effectively released ferulic acid from the cell walls of barley and wheat cell walls than either enzyme alone (see page 208, columns 1 and 2).

It would have been obvious at the time of Applicant's invention to modify the invention of Michelson to combine the ferulic acid encoding polynucleotides and transformation vectors and methods taught in the specification of Michelson with the recombinant expression cassettes taught by Bartolome. One of skill in the art would have been motivated by the teachings of Michelson of the genetic engineering of plants to express a ferulic acid esterase encoding polynucleotide and the success of both Michelson and Bartolome in more effectively releasing ferulic acid and diferulate dimers from grass cell walls when using both ferulic acid esterase and xylanase made from recombinant expression cassettes, and that one would have had a reasonable expectation of success engineering plants to express a ferulic acid esterase and a xylanase; and

wherein using either an inducible, senescence, heat shock, or constitutive promoter, a KDEL ER retention sequence, and a stop codon are obvious optimizations of design parameters and by Applicant's own teachings in the specification that inducible, senescence, heat shock, and constitutive promoters, the KDEL ER retention sequence, and termination sequences are well known in the art (see specification pages 19-21).

Applicant asserts that there is no indication of how recombinant expression of an FAE in plants could be accomplished (response page 13). See arguments supra.

Applicant asserts that there is no motivation other than an obvious to try standard to combine the teachings of the two references (response page 13). Michelson does teach motivation by teaching a plant comprising an expression cassette comprising a ferulic acid esterase encoding polynucleotide in plants derived from *Aspergillus niger*, operably linked to a promoter, taught as an embodiment of the invention.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claim is allowed.

Claims 3-7, 15, 18-19, 30, 32 and 33 are deemed free of the prior art given the failure of the prior art to teach or reasonably suggest Festuca, Lolium, Zea and Avena plants transformed with ferulic acid esterase FAE1 from *Aspergillus* and xylanase from *Trichoderma reesei* encoding polynucleotides using an encoded signal sequence to target gene expression to the vacuole.

AMY J. NELSON, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (571) 272-0798. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Russell Kallis Ph.D.
October 26, 20046